

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicant: DeBenedetti, et al. : Paper No:
Serial No. 10/718,163 : Group Art Unit: 1635
Filed: November 20, 2003 : Examiner: Angell, Jon E.
For: CANCER GENE THERAPY BASED ON TRANSLATIONAL CONTROL OF
A SUICIDE GENE

Confirmation No. 8977

DECLARATION UNDER 37 CFR 1.132

Box Amendment Fee

The Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This declaration under 37 CFR Sec. 1.132 is supportive of the Amendment and Response filed herewith. I, Arrigo DeBenedetti, declare and say:

1. That I am a citizen of Italy, US permanent resident and that I am one of the co-inventors in the above-referenced patent application; that I have been employed by Louisiana State University Health Sciences Center-Shreveport since 1992, that I have been Associate Professor in the Biochemistry Department since 1992, and I was and still am, engaged in a research program in the field of cancer treatment and particularly genetic therapeutics.
2. That I am familiar with the above-identified patent application Ser. No. 10/718,163, that I have reviewed the Office Action, dated February 28, 2008, in the above captioned case, and that I am familiar with the following references cited by the Examiner: Anderson (Nature 1998; 392(suppl):25-30); Crystal (Science 1995; 270:404-410); DeFatta and De Benedetti (*Cancer GeneTherapy* 9:502-512 – 2002); and Kim *et al.* (Trends in Mol. Ned. Vol. 8, Suppl: p. S68-S73; 2002).
3. That I am familiar with the review article Gene Therapy (2003) 10, 453–458, “Progress and prospects: naked DNA gene transfer and therapy” by H Herweijer and JA Wolff and the references cited therein.
4. That the Herweijer and Wolff review shows that many references published prior to the filing date of the present ‘163 application show that increases in efficiency have made naked DNA gene transfer, particularly for in vivo gene transfer, a significantly viable method for gene therapy. That intravascular delivery results in effective gene delivery to liver and muscle, and provides in vivo transfection

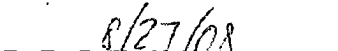
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methods for basic and applied gene therapy and antisense strategies with oligonucleotides and small interfering RNA (siRNA). Delivery via the tail vein in rodents provides an especially simple and effective means for in vivo gene transfer. Electroporation methods significantly enhance direct injection of naked DNA for genetic immunization. The availability of plasmid DNA expression vectors that enable sustained high level expression, allows for the development of gene therapies based on the delivery of naked plasmid DNA.

5. That in view of the references cited in the Herweijer and Wolff review, one skilled in the art would know how to make and use the present invention using other routes of administration, including systemic administration of the therapeutic nucleic acid.
6. That I am familiar with the referenced article by DeFatta and De Benedetti (*Cancer Gene Therapy* 9:502-512 – 2002). That the DeFatta and DeBenedetti article demonstrates that the DNA can also be delivered not only as naked DNA but encapsulated in liposomes and that efficient delivery and transfection of all tissues by systemic administration was demonstrated. Hence, the DNA is also deliverable in a form protected from nucleases in the plasma and immune cells as well known in the art.
7. That in view of the extensive direction and guidance provided, the presence of working examples for in vitro and in vivo gene therapy, the relative breadth of the claims, and the evolved state of the art with respect to gene therapy at the time of filing, practice of the claimed invention would not have required undue experimentation.
8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Further declarant sayeth not.


Arrigo DeBenedetti


Date